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Automatic adjustment of pressure support by a computer-driven knowledge-based system during noninvasive ventilation: a feasibility study

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Abstract *Objective:* To evaluate the feasibility of using a knowledge-based system designed to automatically titrate pressure support (PS) to maintain the patient in a "respiratory comfort zone" during noninvasive ventilation (NIV) in patients with acute respiratory failure. *Design and setting:* Prospective crossover interventional study in an intensive care unit of a university hospital. *Patients:* Twenty patients. *Interventions:* After initial NIV setting and startup in conventional PS by the chest physiotherapist NIV was continued for 45 min with the automated PS activated. *Measurements and results:* During automated PS minute-volume was maintained constant while respiratory rate decreased significantly from its pre-NIV value (20 ± 3 vs. 25 ± 3 bpm). There was a trend towards a progressive lowering of dyspnea. In hypercapnic patients $PaCO_2$ decreased significantly from 61 ± 9 to 51 ± 2 mmHg, and pH increased significantly from 7.31 ± 0.05 to 7.35 ± 0.03. Automated PS was well tolerated. Two system malfunctions occurred prompting physiotherapist intervention. *Conclusions:* The results of this feasibility study suggest that the system can be used during NIV in patients with acute respiratory failure. Further studies should now determine whether it can improve patient-ventilator interaction and reduce caregiver workload.

Keywords Noninvasive ventilation · Pressure support · Knowledge-based system · Automated modes

Introduction

Noninvasive ventilation (NIV) in pressure support mode (PS) has become a standard of care in both hypercapnic and nonhypercapnic acute respiratory failure [1, 2, 3]. Optimization of patient-ventilator interaction is a critical factor determining the success of the technique in avoiding endotracheal intubation [4, 5]. Several key elements have been shown to play an important part in patient-ventilator interaction: discomfort due to either insufficient or excessive levels of PS [6], worsening dynamic hyperinflation in obstructive patients due to excessive PS, and resultant increase in the number of ineffective inspiratory attempts and work of breathing [7, 8]. Furthermore, in acutely decompensated patients this multitasking endeavor carries the risk of both error and suboptimal performance [9, 10].

Recently a closed-loop knowledge-based system implemented in an ICU ventilator designed to automatically adjust the level of PS in intubated patients has demonstrated its ability to improve patient-ventilator interaction [11], assist in the management of weaning [12, 13], and shorten its duration [14]. Theoretically the automatic titration of PS could for the same reasons improve patient-ventilator interaction also during NIV and possibly reduce the clinician's workload. The present pilot study tested the feasibility of applying the closed-loop system during NIV in patients with acute respiratory failure.

Patients and methods

Patients

All patients admitted to the ICU of two university hospitals (University Hospital, Geneva, Switzerland, and St-Luc University Hospital, Brussels, Belgium) for acute respiratory failure and in whom NIV was prescribed were included. Patients were included if they had been treated in the hospital for ≤ 4 h or less and had received at most two NIV applications. Exclusion criteria were the presence of pneumothorax, severe respiratory failure or hemodynamic instability with high probability of imminent intubation, impaired consciousness or absence of patient cooperation, and presence of facial lesions precluding the use of NIV. The study included 20 patients (11 men, 9 women; age 66.5 ± 12.1 years; body mass index 29.7 ± 9.3). Thirteen presented with hypercapnic respiratory failure (eight decompensated chronic obstructive pulmonary disease, two postoperative, one each chronic restrictive disease, pancreatitis, and acute heart failure) and seven with nonhypercapnic respiratory failure (five pneumonia, one sepsis, one following hepatic transplantation). The patients had been treated inhospital for a mean of 17 ± 6 h. Fourteen of the 20 patients had received NIV (mean 1.4 ± 0.5 applications). The protocol was accepted by the Ethics Committee of our institution. Informed consent was obtained from all patients.

Methods

Patients were ventilated with an Evita XL ICU ventilator (Drägerwerk, Lübeck, Germany) in which the evaluated system is embedded and accessible via a touch-screen menu under the commercial name of SmartCare. The knowledge base used to develop this system comes mainly from the scientific literature and from a group of intensivists, physiologists, and scientists. A detailed description of the system has been published elsewhere [12, 15]. Briefly, the system adapts the level of PS to continuously monitored patient data, pursuing the goal of keeping the patient within a respiratory "comfort" zone. The latter is defined as a respiratory rate varying between 15–30 bpm (upper limit 34 in patients with neurological disease), tidal volume above a minimum threshold (300 ml, reduced to 250 ml if patient body weight is < 55 kg), and end-tidal expiratory CO_2 below 55 mmHg (65 mmHg in patients with chronic obstructive pulmonary disease). To reach these targets the level of PS is periodically adapted by the system in steps of 2–4 cmH_2O. The period between evaluations leading to a decision by the system as to whether to change the level of PS is 2 min in the absence of any change in PS, and 5 min if such a change has been made. The first evaluation after the system has been activated occurs after 5 min. Thereafter several additional rules allow the system to manage transient instabilities, suctioning, or hazardous situations. In addition, the system has a second set of rules centered on the goal of automatically attempting to reduce the level of PS down to a minimal level. Briefly, these rules consist of a reduction in the level of PS if a patient has remained in the "comfort zone" for a given period, the duration of which depends on the level of PS. Once the minimal level of PS is attained, if the patient remains in the "comfort zone" at that level, an evaluation period at that minimal level of PS is initiated by the system (equivalent to a spontaneous breathing trial) which if successful leads to an on-screen message recommending extubation. However, this set of rules centered on weaning was inactivated for the present trial as the objective was only to test the feasibility of automatic adjusting PS and not to attempt weaning from mechanical ventilation. Therefore only the automatic titration of PS aiming to maintain the patient in the "comfort zone" was activated.

Criteria for initiating NIV followed our usual practice guidelines which are based on published studies [16, 17] and require that at least two of the following be present: worsening dyspnea over the last 10 days in cases of chronic respiratory failure; respiratory rate above 25/min, arterial pH below 7. 35, $PaCO_2$ higher than 50 mmHg (6.6 kPa), and PaO_2 lower than 50 mmHg (6.6 kPa) determined from arterial blood gas measurements.

All NIV trials were performed by one of the chest physiotherapists involved in the study (A.B. in Geneva, J.R. in Brussels), both highly experienced in the technique and with the SmartCare system. NIV was initially applied with an oronasal mask (adult face mask, Vygon Schweiz, Liebefeld-Bern, Switzerland) in PS mode, the initial settings being: 15 cmH_2O PS, fast pressurization slope (0.1 s), and no positive end-expiratory pressure (PEEP). In all patients airways were humidified with a heat and moisture exchanger (BB100, Pall, East Hills, N.Y. USA). PS was then titrated according to our usual practice guidelines: the level of PS was adjusted to obtain an expired tidal volume of 8 ml/kg and a respiratory rate less than 30/min, with a minimal leak at the mask. In obstructive patients, PEEP was titrated upwards until the number of ineffective inspiratory attempts either disappeared or decreased to below 6/min. In nonobstructive patients a PEEP between 3–6 cmH_2O was used, the level titrated to maintain pulsoxymetry-determined arterial O_2 saturation (SpO_2) at or above 90%. This initial startup period was necessary for several reasons. First, SmartCare requires manual setting of the initial level of PS before it can be activated. Second, given the preliminary nature of the study we wanted to ensure sure that the patients' initial adaptation to NIV was adequate, for which the initial 5-min evaluation period built in the system might not have been appropriate. Third, PEEP in patients with chronic obstructive pulmonary disease is often important to decrease the number of ineffective inspiratory efforts, and its titration is not part of the system's algorithm. Once these targets had been

Table 1 Main respiratory parameters and ventilator settings [*NA* not available, *NIV startup* end of the 10-min initial startup/adaptation NIV period before SC was activated, *pre-NIV* before initiation of noninvasive ventilation, *RR* respiratory rate, *SC* SmartCare driven NIV after 10, 20, 30 and 45 min respectively, *VAS* visual analog scale (0 = no dyspnea, 10 = severe dyspnea), *VTe* expired tidal volume, *VE* minute volume]

	Pre-NIV	NIV startup	SC 10	SC 20	SC 30	SC 45
RR (breaths/min)	25 ± 3	22 ± 5	21 ± 5	21 ± 4	20 ± 3*	21 ± 3
VTe (ml)	NA	686 ± 190	700 ± 200	670 ± 205	735 ± 237	717 ± 205
VE (l/min)	NA	13.1 ± 3.6	12.5 ± 3.3	2.4 ± 3.2	12.8 ± 3.1	13.4 ± 2.8
Dyspnea (VAS points)	3.2 ± 1.7	2.8 ± 1.6	2.2 ± 1.1	2.2 ± 1.1	2.1 ± 0.9	2.0 ± 1.0
Pressure support (cmH_2O)	NA	17 ± 3	18 ± 4	16 ± 5	17 ± 5	16 ± 5
FIO_2	0.32 ± 0.02	0.28 ± 0.05	0.29 ± 0.04	0.31 ± 0.03	0.28 ± 0.04	0.28 ± 0.04
PEEP (cmH_2O)	NA	5 ± 0.3	5 ± 0.4	5 ± 0.3	5 ± 0.3	5 ± 0.4
Leaks[a]	NA	23 ± 5	22 ± 4	24 ± 6	20 ± 4	21 ± 3

* $p < 0.05$ vs. pre-NIV (analysis of variance)
[a] Reported by the ventilator, expressed as a proportion of VE: (VTi − VTe)/VTi, where VTe = expired tidal volume and VTi = inspired tidal volume

attained, the initial startup period was considered over, and the SmartCare system was activated and NIV pursued for 45 min. The therapist remained at the bedside during the entire procedure and manually adjusted the level of PS, PEEP, FIO_2, or mask fitting in the case of obvious patient-ventilator asynchrony or discomfort, if SpO_2 decreased to less than 88%, or respiratory rate increased to above 30 for more than 3 min. All changes performed were then recorded automatically in the machine's log. After 45 min NIV was discontinued. If patients required further NIV sessions, the technique was applied without the SmartCare system. The following parameters were recorded before the start of NIV (pre-NIV), at the end of the startup/adaptation period (NIV startup), and after 10, 20, 30, and 45 min of NIV using SmartCare (SC 10, SC 20, SC 30, SC 45): respiratory rate, expired tidal volume, minute volume, leaks at the mask [(VTi – VTe)/VTi, where VTe = expired tidal volume and VTi = inspired tidal volume), arterial blood gases (not performed at 10 and 30 min), SpO_2 and end-tidal expired CO_2 measured at the mask (both continuously recorded), dyspnea (visual analog scale), heart rate, and arterial blood pressure.

Statistics

All results are expressed as mean (± SD). The six time-points were compared by analysis of variance (SigmaStat 2.0, SPSS Science), with significance between the time points being determined by Fisher's protected least significance test. A p value of less than 0.05 was considered statistically significant.

Results

The end of the startup/adaptation period with conventional PS was achieved after 10 ± 4 min. Ventilator settings at the end of that period were: level of PS 17.2 ± 3 cmH_2O, PEEP 5 ± 0.7 cmH_2O, and FIO_2 0.29 ± 0.04. The main respiratory parameters and course of ventilator settings are summarized in Table 1. During the 45 min of SmartCare NIV minute volume and tidal volume were stable while respiratory rate slowly declined, reaching statistical significance compared to its pre-NIV value after 30 min. Concomitantly there was a trend towards a decrease in dyspnea. The PS level was maintained fairly constant by the system. The individual variations in PS as set by the system are shown in Fig. 1. During the 45-min period there were no changes in PS in six patients, one automatic change in six other patients, and more than one automatic change in eight (two in six patients and three changes in two).

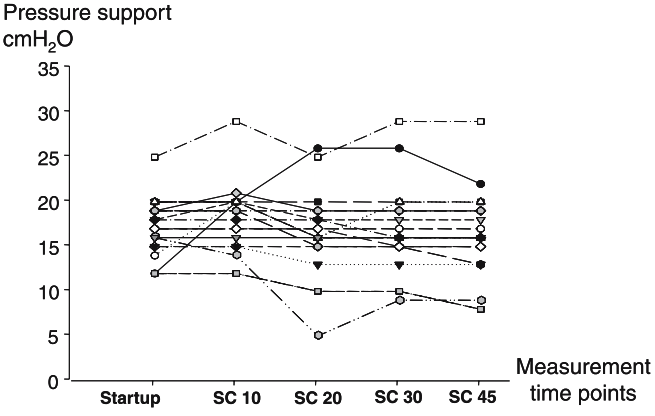

Fig. 1 Individual variations in the level of pressure support during SmartCare-driven NIV. *NIV startup* End of the 10-min initial startup/adaptation NIV period before SC was activated; *SC 10*, *SC 20*, *SC 30*, *SC 45* measurements performed after 10, 20, 30, and 45 min of SmartCare driven NIV, respectively

Table 2 summarizes the course of arterial blood gases and hemodynamics. There was a trend towards a decrease in $PaCO_2$ in the group of patients as a whole, which was

Table 2 Arterial blood gases and hemodynamics ($ETCO_2$ end-tidal CO_2, *HR* heart rate, *MAP* mean arterial pressure, *NA* not available, *NIV startup* end of the 10-min initial startup/adaptation NIV period before SC was activated, PaO_2 arterial partial pressure of O_2, PaO_2/FIO_2 ratio of arterial partial pressure of O_2 to inspired O_2 fraction, $PaCO_2$ arterial partial pressure of CO_2)

	Pre-NIV	NIV startup	SC 10	SC 20	SC 30	SC 45
pH						
All	7.37 ± 0.06	7.38 ± 0.06	NA	7.38 ± 0.05	NA	7.39 ± 0.04
Acidotic[a]	7.31 ± 0.05	7.32 ± 0.02	NA	7.34 ± 0.03	NA	7.35 ± 0.03*
$PaCO_2$ (mmHg)						
All	50 ± 11	44 ± 8	NA	44 ± 9	NA	43 ± 6
Hypercapnic[b]	61 ± 9	57 ± 4	NA	54 ± 3*	NA	51 ± 2*
PaO_2 (mmHg)	73 ± 15	75 ± 11	NA	75 ± 13	NA	77 ± 14
PaO_2/FIO_2	228 ± 28	267 ± 21	NA	241 ± 23	NA	275 ± 18
$ETCO_2$ (mmHg)						
All	NA	29 ± 7	30 ± 8	29 ± 6	29 ± 7	30 ± 7
Hypercapnic[b]	NA	33 ± 7	35 ± 6	34 ± 6	34 ± 5	33 ± 6
HR (bpm)	88 ± 16	87 ± 13	84 ± 16	83 ± 19	85 ± 12	85 ± 13
MAP (mmHg)	82 ± 15	81 ± 10	80 ± 11	80 ± 10	82 ± 10	81 ± 10

* $p < 0.05$ vs. pre-NIV (analysis of variance)
[a] Defined as initial pH < 7.35
[b] Defined as a $PaCO_2 \geq 45$ mmHg

significant in the hypercapnic patients after 20 min of SmartCare NIV. This was accompanied by a significant increase in pH in patients who were initially acidotic. Likewise, in the two patients whose initial pH was higher than 7.45, pH decreased from 7.52 to 7.45 and from 7.45 to 7.42, respectively.

Two problems were encountered that were directly linked to the system. In one patient the end-tidal CO_2 ($ETCO_2$) sensor malfunctioned, exhibiting values in turn above and below the threshold, which led to erratic PS settings and poor patient tolerance. The problem subsided after the sensor was changed. In another patient the respiratory rate recorded by the system was higher than that of the patient, leading to an unnecessary increase in the PS level. The problem was solved by rebooting the system. No other outside intervention from the therapist was required other than improving mask fitting. In no patient was the 45-min NIV trial discontinued because of intolerance or malfunction.

Discussion

The results of this study show that it is possible to perform NIV using a closed-loop knowledge-based system designed to automatically titrate the level of PS with the goal of optimizing weaning from mechanical ventilation in intubated patients. Before discussing the implications of these results, let us first examine the limitations of this study.

First, this was a feasibility study designed to test whether the knowledge-based system could be applied to NIV during a single 45-min trial. Therefore no conclusion can be drawn as to how it compares to NIV conducted by an ICU nurse or respiratory therapist nor about any impact it might have on patient outcome. The duration of NIV application was, however, in line with that reported in other studies [18, 19, 20]. Second, the system's algorithms are designed to combine automatic PS setting and a weaning strategy in intubated patients. Therefore its application to NIV would require the development of rules and settings tailored to the specific aspects of that technique and their clinical validation. Third, the therapists conducting NIV were part of the investigating team, which could introduce bias in the results. However, for safety reasons it was deemed mandatory that the SmartCare NIV trial be supervised by a person highly trained and experienced with the system. Likewise, a rapid initial startup/adaptation NIV phase by an experienced therapist was important so that the system could be applied in patients who were not entirely stabilized after a prolonged period on NIV. Furthermore, a written record was required for all changes made in ventilator settings during the 45-min SmartCare NIV trial, and no intervention other than the two required by system problems were needed. That said, mask adjustments were performed by the therapist, and this certainly contributed to the fairly low level of leaks documented. Severe leaks might interfere with the systems algorithm, and the precise impact of leaks on its overall performance should be explored if its application to NIV were to be pursued. Finally, the patient group was small and heterogeneous. Nonetheless, the diagnostic categories were representative of the usual cause for which NIV is required in the acute setting [2].

The main message of this study is that it is possible to conduct NIV using an algorithm designed to automatically titrate the level of PS to maintain the patient within a predefined respiratory "comfort zone." The system

proved capable of maintaining an adequate minute-volume while the patients' respiratory rate declined, a response which has been documented in patients with both hypercapnic and nonhypercapnic respiratory failure undergoing conventional NIV. During the 45-min trial patients were maintained within the limits defining the "comfort zone." These results are encouraging and are in line with those of two previous studies showing that the system can maintain intubated patients within these limits during periods ranging from 24 h [11] to 12 days [13]. However, the two system malfunctions encountered, both requiring the therapist's intervention, should be kept in mind. Indeed, while quickly solved, these problems were a source of patient-ventilator asynchrony, precisely what one might hope to alleviate with automated systems such as SmartCare. These problems underline the need for further development of this product if it should be considered for NIV use.

The reduction in $PaCO_2$ documented in the hypercapnic patients was also in line with results from other studies in comparable patients [18, 19]. The level of PS measured at the various time points was close to that reached at the end of the startup/adaptation period and is within the range usually reported in acute NIV [18, 21]. Interestingly, the $ETCO_2$ showed little change during the study and exhibited a large gap compared to $PaCO_2$. This finding is not very surprising given the presence of leaks that are expected to alter $ETCO_2$ readings and underline the lack of appeal in using $ETCO_2$ as a monitoring tool during NIV.

If future studies confirm the feasibility of using this system on a larger scale during NIV, it could prove useful in the management of acutely decompensated patients for several reasons. First, by avoiding insufficient and excessive levels of PS, both a source of major discomfort [6], patient tolerance could be improved, which is a key factor in the success of the technique in avoiding intubation [4, 5]. Second, in obstructive patients excessive levels of PS can lead to worsening dynamic hyperinflation, in turn resulting in an increase in the number of ineffective inspiratory attempts [8]. Avoiding such high levels could therefore avoid unnecessary increases in the work of breathing associated with this condition [7]. Finally, applying NIV in the acute setting implies that the clinician's attention be divided between the proper setting of ventilator parameters, minimizing leaks at the mask-patient interface, and continuously monitoring vital parameters, all the while attempting to comfort an often agitated and anxious patient. Such multitasking performed in acute and stressful conditions is a well-recognized contributing factor to the occurrence of incidents [9, 10]. Automation of some of the tasks associated with NIV could help reduce some of these risks [10], provided that the algorithms used are robust and safe enough.

In conclusion, the present study demonstrates the feasibility of using a commercially available knowledge-based system to automatically titrate the level of PS during NIV in patients with acute respiratory failure. Although clearly not a validation of the concept of using such a system in routine clinical practice at this stage, these results suggest that future studies should now be conducted, initially focusing on: (a) the design and validation of specific rules for the use of SmartCare during NIV and (b) whether the system compares favorably to conventionally titrated PS, and proves beneficial in terms of caregiver workload and improved patient tolerance.

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